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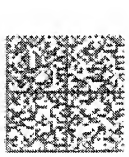

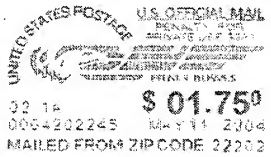

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,961	11/26/2003	Thomas P. Blackburn	62163-AA/JPW/ANX	2139

7590 05/11/2004

John P. White
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036

EXAMINER	
PATEL, SUDHAKER B	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 05/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/723,961	BLACKBURN ET AL.	
	Examiner	Art Unit	
	Sudhaker B. Patel, D.Sc.Tech.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *256-271* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *256-271* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 November 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/26/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' communication paper dated 11/26/03 is acknowledged.

Applicants have cancelled claims 1-255, and presented new claims 256-271, which are related as compounds, composition, method of making composition, and method of treating diseases respectively. The claims in this application are the claims 256-271.

First action on merits follows.

Priority

1. This application filed under former 37 CFR 1.60 lacks the necessary reference to the prior application. A statement reading "This is a **continuation of U. S. Application Sr. No.** 10066175, filed 1/31/02, now ABN, which claims **Priority from Provisional Application** 60265586 filed 1/31/01. . ." should be entered following the title of the invention or as the first sentence of the specification. Also, the current status of all nonprovisional parent applications referenced should be included.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on 11/26/03 is being considered by the examiner. Signed copy of PTO Form 1449 is enclosed with this communication for applicants' record.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. . Claims 256-271 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply.

5. Claim 256 recite 'A" component as:" Oxazolyl, thiazolyl, triazolyl, triazinyl...".These are not exact and definite structures because each terms has isomers, and therefore, their exact point of attachment to the main core has been excluded from claim recitation. Correction is required.

6. Claim 268 is objected to because of the following informalities: If claim 267 is allowed, claim 268 will be duplicate composition claim. Appropriate correction is required.

7. Claim 269 is related to the process of making a pharmaceutical composition. Claim remains silent by not reciting the exact process or steps required for making the composition.

8. Compounds recited by an independent Claim 264 cannot be accommodated by the Formula of main claim 256 for the definitions recited for B component. Claim 256 remains silent about the hydrogenated form of phenyl i.e. cyclohexyl group.
9. Claims 270-271 recite method of treating a subject suffering from a disease(s), which are not exactly and definitely defined. What is excluded from the term" subject"? The claims remain silent about the exact amount of the compound of claims 256, and also about the definite and exact process of administration. Claims also do not state anything about the pharmacological properties inherent to compounds. Correction(s) are required.
10. The specification page 606 is repeated twice, and page608 is missing. Correction is required.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 270-271 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a single, definite and exactly defined disease, does not reasonably provide enablement for generic subject's disorder(s) related to depression & anxiety. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification in pages 1-3 describe **depression** as one of the mental bipolar disorders characterized by sad ness, flatness, loss of feeling, anhedonia, tearfulness, anxious or agitated state, agitation or retardation, thoughts of guilt and worthness. **Anxiety** disorders are related to various combinations of psychological and physical manifestations of anxiety, or other obessional & hysterical symptoms which are clinically nondominating neurotic features. Additionally, depression or anxiety also meets the criteria for at least one other psychiatric disorder.

(1). In cases directed to chemical compounds, which are being used for their physiological/biological activity, the scope of the claims must have a reasonable correlation to the scope of enablement provided by the specification. See in re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group and In re Wiggins 179 USPQ 421.

(2). " Compounds, their esters with –COOR$, Amides with –NHCOR4 or –CON (R4) 2, pharmaceutical salts, Pharmaceutical compositions thereof, consisting of compound(s) of claim256, 264 with one or more receptor antagonists "as recited in the specification read on all such moieties regardless of complexity of structure and point of attachment to the aliphatic or carbocyclic or aromatic or heterocyclic core or bridge/chain for which there is no sufficient teaching how to make and how to use at any one selective location among the many possible sites present. The situation is more

confusing when a skilled person in the art tries to visualize the multiple possibilities of combining a compound of claim 256(or claims dependent on it) and/ or its composition in combination with other pharmacologically acceptable carrier ". Applicants provide no reasonable assurance that any and all compositions of the instant compounds and their combinations either alone or in a combination as outlined, will have ability to generate the compounds in vivo or in vitro by one or more processes.

13. In evaluating the enablement question, several factors are to be considered. In re Wands, 8 USPQ 2d 1400 (Fed. Cir. 1988); Ex parte Forman, 230 USPQ 546. The factors include:***(1).*** The nature of invention;***(2).*** the state of prior art ;***(3).*** the predictability or lack thereof in the art; ***(4).*** the amount of direction or guidance present;***(5).*** the presence or absence of working examples;***(6).*** the breadth of the claims, and ***(7).*** the quantity of experimentation needed.

14. **1) The nature of the invention:** The method of use claims are drawn in part to treating of diseases related to depression and anxiety. The diseases include **depression** as one of the mental bipolar disorders characterized by sad ness, flatness, loss of feeling, anhedonia, tearfulness,anxious or agitated state, agitation or retardation, thoughts of guilt and worthness**. Anxiety** disorders are related to various combinations of psychological and physical manifestations of anxiety, or other obessional & hysterical symptoms which are clinically nondominating neurotic features. Additionally, depression or anxiety also meets the criteria for at least one other psychiatric disorder.

2) The state of the prior art: There are no known compounds of similar structure which have been demonstrated for treating these complex diseases by a single compound. These diseases involve part of the CNS system consisting of different receptors in the body. For example, cocaine binds at the dopamine reuptake transmitter. Heroin addiction, for example, arises from binding at the opiate receptors, cigarette addiction from some interaction at the nicotinic acid receptors, many tranquilizers involve the benzodiazepine receptor, alcohol involves yet another system, etc. All attempts to find a pharmaceutical to treat chemical addictions generally have thus failed. Alzheimer's disease, which is CNS, related disease is treatable, albeit not successfully, using acetylcholine esterase inhibitors and Parkinson's disease using dopamine receptors. A disease in the central or peripheral system is not a single disease but embraces diseases that are not related or even "opposites".

3) The predictability or lack thereof in the art: It is presumed in the treatment of the diseases claimed herein there is a way of identifying any and all of the diseases which are responsive to the activity of GAL3 antagonist receptors. There is no evidence of record, which would enable the skilled artisan in the identification of the diseases treatable with the disorders claimed herein.

4) The amount of direction or guidance present and 5) the presence or absence of working examples: There are no doses or patient-dosage regime present for treatment of the disorders recited.

6) The breadth of the claims: The claims are drawn to disorders that are not related and whose treatment mechanism is relatively unknown.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan for the many reasons stated above.

Following references are cited to show the state of art related to a few of the diseases recited herein:

- **Developments in treatment of anxiety disorders:psychotherapy,pharmacecotherapy, and psychosurgery:**

Balon R.(PubMed Abstract 15022141, also cited as Depress. Anxiety, 19/2,63-76(2004)) state that:" A combination of proven pharmacotherapy and psychotherapies may be most clinically prudent approach to the treatment of anxiety disorders....In spite of all the research and progress in studying relatively well defined therapies, many patients suffering from anxiety and depression still .... Complementary and alternative therapies".

- **Omega-3-fatty acids for prevention of postpartum depression:**

Marangell et al(PuibMed Abstract 14978781, also cited as Depress. Anxiety, 19/1,20-3(2004)) state that:" This preliminary, small, open-label pilot study failed to show promising results for the use of omega-3 fatty acid monotherapy beginning at 34 to 36 weeks gestation for prevention of postpartum depression in patients with a poor postpartum depression history". No such studies have been conducted and described in the specification.

- **Mode of administration-Intravenous antidepressants:**

Moukaddam et al(PubMed Abstract 14978779, also cited as Depress. Anxiety. 19/1,1-9(2004)) state that:" The controlled studies on i.v. administration of anti-depressants, clomipramine, citalopram, and other antidepressants do not support increased efficacy for i.v. over p.o. administration but there are suggestions of a faster onset action".

- **Nonpeptide vasopressin receptor antagonists:**

Serradeil et al(PubMed Abstract 12436936, also cited as Prog. Brain Res., 139,197-210(2002)) state that:" In conclusion, the development of AVP receptor antagonists is a field of intensive pharmacological and clinical investigation. Selective and orally active compounds are now available to give new insight into the pathophysiological role of AVP and to provide promising drugs". Specification does not provide such data for the instant compounds and compositions.

15. Specification on pages 11-13 recite various methods of assays and tests carried out by the applicants for the instant compounds.

On pages 3-7 summarize the pathologies of depression/anxiety from the experiments carried out with animals but not with human for which the instant claims are recited.

Op pages 597-606 specification describes various method used for testing binding properties of compounds cloned receptors, and results for the binding affinities and selectivity ratios are illustrated in Tables 7-10 as recited in pages 606-611.

On pages 612-625 specification describes the assays/tests carried out for GAL3 receptor localization. Conclusion in page 625, lines 5-15 states that:" GAL3 has been identified in all of these regions and thus presents itself as a potential therapeutic targets in the treatment of depression".

These results are not sufficient to support the methods of use claims claiming treating depression as well as anxiety in a generic way. These results will help as a preliminary guideline for screening the compounds only.

16. Statements of utility, which relate to or imply to treatment of a disease are subject to closer scrutiny. Ex parte Moore et al.(POBA 1960) 128 USPQ 8. Claims do not meet the Utility Guidelines. The claims do not qualify as one utility statement, and are not believable on their face. Claims will require too much experimentation to determine what patient dosage relationship would produce what results. It is not believable on its face that any one compound would have all of those utilities. In re Hozumi, 226 USPQ 353.

The quantity of experimentation need would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan for the many reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skilled in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the

instant case for the instant method claims involving use of compounds, their compositions.

17. When the best efforts have failed to achieve a goal, it is reasonable for the PTO to require evidence that such a goal has been accomplished, *In re Ferens*, 163 USPQ 609. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006.

Conclusion
Allowable Subject Matter

15. Claims 256-269 related to compounds, composition, and aprocess of making compositions would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, and other rejections, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

16. Method of use claim related to a single, specific and definite disease would also be considered for allowance provided applicants submit supporting evidence by way of experimental data.

17. The following is a statement of reasons for the indication of allowable subject matter: The closest prior art(s) ref. Ei-Ezbawy et al(Chemical Asbstract DN 112:178540, also cited as P, S, & Si & the related Elements,44/3-4,285-9(1989) teaches making of compounds with a core:"2H-Indol-2-one, 3-(substituted phenyl)imino-1,3-duhydro-1-(heterocycle = morpholine). The instant claims differ from the above cited reference by having different substituents on to position 1 nitrogen, and also onto the phenyl groups.

18. The other reference Abdel-Rahman et al(Chemical Abstract DN 109:190175, also cited as J. of the Chem. Soc. Of Pakistan, 9/4,523-37(1987) teaches making of compounds of Formula I wherein H of NH of indole can be replaced by a heterocycle other than instantly claimed, and ref. R1 group can be aliphatic, heterocycle or substituted phenyl.

19. The references either alone or in combination do not suggest or indicate to arrive at the instantly claimed compounds.

20 Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhaker B. Patel, D.Sc.Tech. whose telephone number is (571) 272-0671.

The examiner can normally be reached on 6:30 to 5:00 pm (Monday-Thursday). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund J. Shah can be reached on (571) 272 0674 or Sr. Examiner Mr. Richard Raymond at (571) 272 0673 or Mr. James O. Wilson at (571) 272-0661.

The fax phone numbers for the organization where this application or proceeding is assigned are 703 308 4556 for regular communications and 703 308 4556 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1235.Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sudhaker B. Patel, D.Sc. Tech.
May 5, 2004

RICHARD L. RAYMOND
PRIMARY EXAMINER
ART UNIT 1624

MUKUND J. SHAH
SUPERVISORY PATENT EXAMINER
ART UNIT 1624/1623

Form PTO-1449 U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 1795/62163-AA/ JPW / ANX	Serial No. Not Yet Known 10723961
INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)	Applicants Thomas Blackburn, et al.	
	Filing Date Herewith 11/26/03	Group Art Unit ~~Not Yet Known~~ 1624

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Examiner Initial		Document Number							Date	Name	Class	Subclass	Filing Date if Appropriate
8B	US	5	8	4	0	8	9	3	11/24/98	Bukrinsky, et al.	—	—	—
	US	5	8	0	1	1	5	0	9/1/98	Caillot, et al.	—	—	—
	US	5	7	2	8	7	0	4	3/17/98	Mylari, et al.	—	—	—
	US	5	5	4	7	9	4	9	8/20/96	Maho, et al.	—	—	—
	US	5	0	1	7	4	6	6	5/21/91	Kobayashi, et al.	—	—	—
	US	4	9	2	1	5	0	3	5/1/90	Anderson, et al.	—	—	—
	US	4	8	7	4	6	8	7	10/17/89	Itabashi, et al.	—	—	—
	US	4	9	4	6	9	5	6	8/7/90	Wheeler, et al.	—	—	—
8B	US	6	3	6	8	8	1	2	4/9/02	Bard, et al. *	—	—	—

FOREIGN PATENT DOCUMENTS

		Document Number							Date	Country	Class	Subclass	Translation Yes	Translation No
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	WO	9	9	5	0	2	5	0	10/7/99	PCT	—	—	—	—
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	WO	9	3	2	5	5	3	9	12/23/93	PCT	—	—	—	—
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8B	JP	11	1	5	8	0	7	3	6/22/77	Japan	—	—	—	—

EXAMINER [signature]	DATE CONSIDERED 5/4/04

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Applicants: Thomas P. Blackburn, et al.
U.S. Serial No.: Not Yet Known
Filing Date: Herewith

Exhibit A

Form PTO-1449 U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 1795/62163-AA/JPW/ANX	Serial No. Not Yet Known
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	Filing Date Herewith	Group Art Unit Not Yet Known

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		Hokfelt, T., et al., "Galanin and NPY, Two Peptides with Multiple Putative Roles in the Nervous System," Horm. Metab. Res. (1999); 31: 330-334;
		Razani, H., et al., "Intraventricular Galanin Produces a Time-Dependent Modulation of 5-HT1A Receptors in the Dorsal Raphe of the Rat", Neuropharmacology and Neurotoxicology. (2000); 11(18): 3943-3948;
		Chemical Abstracts Registry No. 61038-64-0;
		Chemical Abstracts Registry No. 41230-77-7;
		Chemical Abstracts Registry No. 130186-15-1;
		Chemical Abstracts Registry No. 130186-16-2;
		Chemical Abstracts Registry No. 130186-17-3;
		Chemical Abstracts Registry No. 130186-18-4;
		Chemical Abstracts Registry No. 130186-21-9;
		Chemical Abstracts Registry No. 130270-13-2;
		Chemical Abstracts Registry No. 133939-75-0;
		Chemical Abstracts Registry No. 56984-58-8;
		Chemical Abstracts Registry No. 77910-42-0;
		Chemical Abstracts Registry No. 70010-41-2;
		Chemical Abstracts Registry No. 189264-35-5;
		Chemical Abstracts Registry No. 88291-04-7;
		Chemical Abstracts Registry No. 88291-07-0;
		Chemical Abstracts Registry No. 154118-05-5;
		Chemical Abstracts Registry No. 155717-81-0;
		Chemical Abstracts Registry No. 155717-82-1;
		Chemical Abstracts Registry No. 159967-24-5;

EXAMINER [signature] DATE CONSIDERED 5/4/04

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	Filing Date Herewith	Group Art Unit Not Yet Known

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		Chemical Abstracts Registry No. 138601-94-2;
		Chemical Abstracts Registry No. 136647-69-3;
		Chemical Abstracts Registry No. 136647-72-8;
		Chemical Abstracts Registry No. 77297-28-0;
		Chemical Abstracts Registry No. 43002-26-2;
		Chemical Abstracts Registry No. 303954-69-2;
		Chemical Abstracts Registry No. 122725-53-5;
		Chemical Abstracts Registry No. 122803-89-8;
		Chemical Abstracts Registry No. 303149-10-2;
		Chemical Abstracts Registry No. 303149-08-8;
		Chemical Abstracts Registry No. 303149-06-6;
		Chemical Abstracts Registry No. 303984-47-6;
		Chemical Abstracts Registry No. 303149-14-6;
		Chemical Abstracts Registry No. 303149-12-4;
		Chemical Abstracts Registry No. 303984-51-2;
		Chemical Abstracts Registry No. 303984-49-8;
		Chemical Abstracts Registry No. 303954-48-7;
		Chemical Abstracts Registry No. 303984-52-3;
		Chemical Abstracts Registry No. 303984-60-3;
		Chemical Abstracts Registry No. 303984-61-4;
		Chemical Abstracts Registry No. 303984-62-5;
		Chemical Abstracts Registry No. 303984-68-1;
		English Language Abstract for Japanese Patent No. JP 11,158,073;
		U.S. Serial No. 10/214,873 (Konkel et al.), filed August 7, 2002; NOW ABN
		U.S. Serial No. 10/066,175, filed January 31, 2002, (Exhibit 1). NOW ABN

EXAMINER	DATE CONSIDERED
	5/4/04

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	Examiner Sudhaker B. Patel, D.Sc.Tech.	Art Unit 1624	Page 1 of 2

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NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Chemical Abstract DN 112:178540, also cited as PSSLEC;ISSN:1042-6507, P,S,& SI & the related Elements,44/3-4,285-9(1989).
	V	Chemical Abstract DN 109:190175, also cited as J. Chem. Soc. of Pakistan, 9/4,523-37(1987).
	W	PubMed Abstract 15022141.
	X	PubMed Abstract 14978781.

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Notice of References Cited	Application/Control No. 10/723,961	Applicant(s)/Patent Under Reexamination BLACKBURN ET AL.	
	Examiner Sudhaker B. Patel, D.Sc.Tech.	Art Unit 1624	Page 2 of 2

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-			
	B	US-			
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	P					
	Q					
	R					
	S					
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NON-PATENT DOCUMENTS

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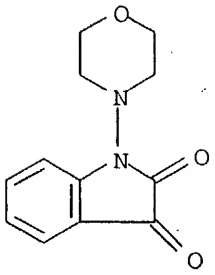
	U	PubMed Abstract 14978779. ✓
	V	PubMed Abstract 12436936. ✓
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

L3 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:178540 CAPLUS
DN 112:178540
TI Synthesis and biological activities of new indole derivatives containing sulfide and/or sulfone moieties. Part I
AU El-Ezbawy, Samia R.; Abdel-Wahab, Aboel Magd A.
CS Fac. Sci., Assiut Univ., Assiut, Egypt
SO Phosphorus, Sulfur and Silicon and the Related Elements (1989), 44(3-4), 285-9
CODEN: PSSLEC; ISSN: 1042-6507
DT Journal
LA English
OS CASREACT 112:178540
IT **126592-64-1**, 1-Morpholinoisatin
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with aminophenyl nitrophenyl sulfides)
RN 126592-64-1 CAPLUS
CN 1H-Indole-2,3-dione, 1-(4-morpholinyl)- (9CI) (CA INDEX NAME)



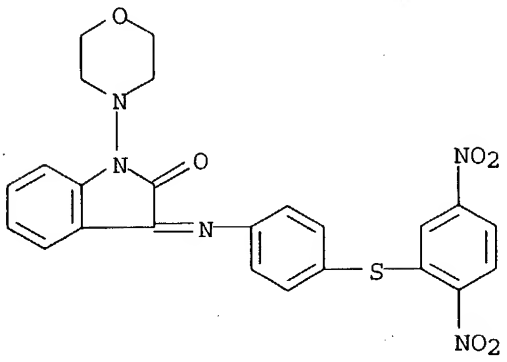
IT **126592-73-2P 126592-74-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

Patel <5/4/2004>

(preparation and antibacterial activity of)

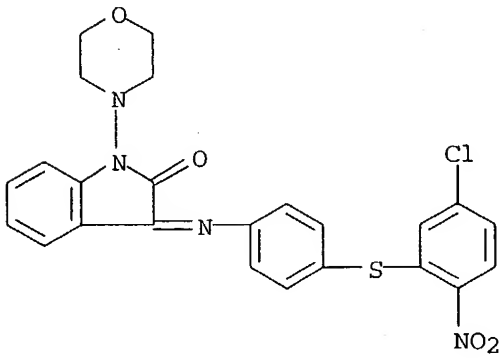
RN 126592-73-2 CAPLUS

CN 2H-Indol-2-one, 3-[[4-[(2,5-dinitrophenyl)thio]phenyl]imino]-1,3-dihydro-1-(4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 126592-74-3 CAPLUS

CN 2H-Indol-2-one, 3-[[4-[(5-chloro-2-nitrophenyl)thio]phenyl]imino]-1,3-dihydro-1-(4-morpholinyl)- (9CI) (CA INDEX NAME)



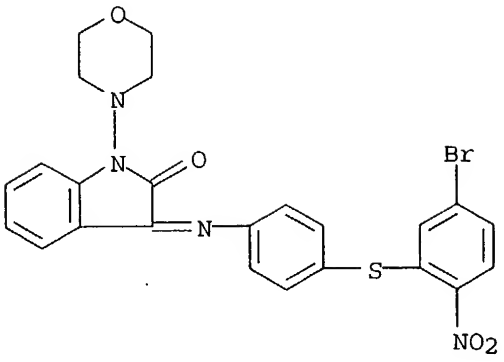
IT **126592-75-4P 126592-76-5P**

RL: SPN (Synthetic preparation); PREP (Preparation)

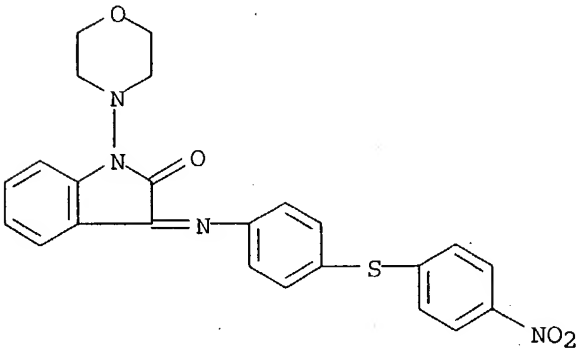
(preparation of)

RN 126592-75-4 CAPLUS

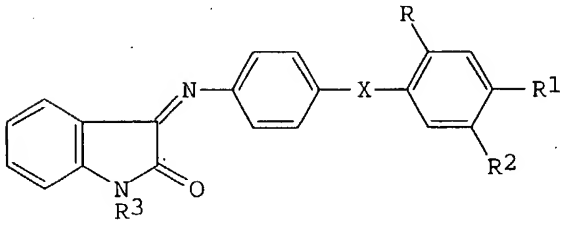
CN 2H-Indol-2-one, 3-[[4-[(5-bromo-2-nitrophenyl)thio]phenyl]imino]-1,3-dihydro-1-(4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 126592-76-5 CAPLUS
CN 2H-Indol-2-one, 1,3-dihydro-1-(4-morpholinyl)-3-[[4-[(4-nitrophenyl)thio]phenyl]imino]- (9CI) (CA INDEX NAME)



GI



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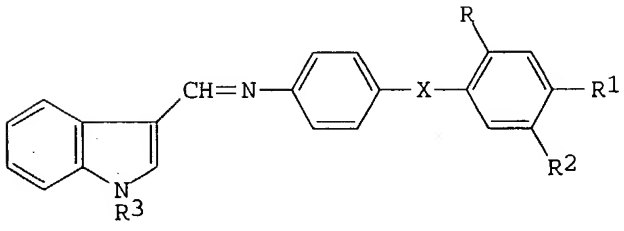
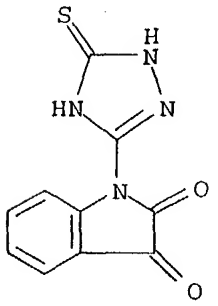


II

AB 2,4,5-RR1R2C6H2XC6H4NH2-4 (R,R1 = H, NO2; R2 = NO2, Cl, Br, H; X = S, SO2) react with isatin, N-acetylisatin, isatin-N-Mannich bases, indole-3-carboxaldehyde and N-substituted indole-3-carboxaldehyde producing the corresponding indole derivs. I (R3 = H, MeCO) and II [R3 = H, 2,4-(O2N)2C6H3, 4-O2NC6H4CO]. A screen of these compds. for antibacterial activity showed most of the tested compds. possessed strong activity aganist a variety of bacteria.

AN 1988:590175 CAPLUS
DN 109:190175
TI Some reactions with 2(3)-indolone derivatives
AU Abdel-Rahman, R. M.; Abdel-Halim, A. M.; Ibrahim, S. S.; Mohamed, E. A.
CS Fac. Educ., Ain Shams Univ., Cairo, Egypt
SO Journal of the Chemical Society of Pakistan (1987), 9(4), 523-37
CODEN: JCSPDF; ISSN: 0253-5106
DT Journal
LA English
OS CASREACT 109:190175
IT **116957-62-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 116957-62-1 CAPLUS
CN 1H-Indole-2,3-dione, 1-(2,5-dihydro-5-thioxo-1H-1,2,4-triazol-3-yl)- (9CI)
(CA INDEX NAME)



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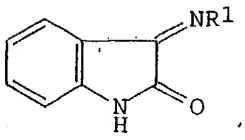

I

AB Isatin condensation products I [R1 = CH2CH2OH, 4-pyridyl, 2-O2NC6H4, 4-BrC6H4, NH2, PhCH:CHCH:N, C(:NH)NHCN, 4-AcNHC6H4SO2NH, MeCONH, PhCONH] were prepared A mixture of isatin and 2-O2NC6H4NH2 in EtOH was heated to give I (R1 = 2-O2NC6H4).

2: Depress Anxiety. 2004;19(2):63-76.

Developments in treatment of anxiety disorders: psychotherapy, pharmacotherapy, and psychosurgery.

Balon R.

Department of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, Detroit, Michigan, USA. Rbalon@wayne.edu

A selection of articles that focus on psychosocial treatments, pharmacotherap and psychosurgery of anxiety disorders are reviewed. While some medicatio look clearly beneficial or potentially effective in the treatment of anxiety disorders, other compounds seem less promising or not effective. A combina of proven pharmacotherapies and psychotherapies may be the most clinically prudent approach to the treatment of anxiety disorders. Thermocapsulotomy be an "extreme" option in selected cases of severe nonobsessive anxiety but i carry a significant risk of adverse effects indicative of frontal lobe functionin impairment. In spite of all the research and progress in studying relatively we defined therapies, many patients suffering from anxiety and depression still u complementary and alternative therapies. The use of alternative and complementary is likely to increase as insurance coverage expands. Copyrigl 2004 Wiley-Liss, Inc.

PMID: 15022141 [PubMed - in process]

3: Depress Anxiety. 2004;19(1):20-3. Related Articles,

InterScience

Omega-3 fatty acids for the prevention of postpartum depression: negative data from a preliminary, open-label pilot study.

Marangell LB, Martinez JM, Zboyan HA, Chong H, Puryear LJ.

Department of Psychiatry, Baylor College of Medicine, Houston, Texas 770 USA. laurenm@bcm.tmc.edu

Based on the putative relationship between depleted omega-3 fatty acids and postpartum depression, we initiated an open-label pilot study of omega-3 fatt acid supplementation with the aim of preventing postpartum depression. Euthymic pregnant females with a past history of depression in the postpartu period were started on 2960 mg of fish oil (1.4:1 eicosapentaenoic acid:docosahexaenoic acid) per day between the 34th to 36th week of pregna and assessed through 12 weeks postpartum. Four of seven participants had a depressive episode during the study period. No participants withdrew from th study due to adverse events. This preliminary, small, open-label pilot study failed to show promising results for the use of omega-3 fatty acid monothera beginning at 34 to 36 weeks gestation for the prevention of postpartum depression in patients with a prior postpartum depression history. Controlled studies are lacking. Copyright 2004 John Wiley & Sons, Ltd.

PMID: 14978781 [PubMed - in process]

111

4: Depress Anxiety. 2004;19(1):1-9. Related Articles,

InterScience

Intravenous antidepressants: a review.

Moukaddam NJ, Hirschfeld RM.

University of Texas Medical Branch at Galveston, Galveston, Texas 77555, USA. njmoukad@utmb.edu

Antidepressant medications have an onset of action of several weeks and hav moderate efficacy. Their mode of administration is oral (p.o.). Some clinician wondered whether intravenous (i.v.) administration would speed onset of act and increase efficacy. In this article we review controlled studies on i.v. administration of antidepressants. These include clomipramine, citalopram, a other antidepressants. Overall these studies do not support increased efficacy i.v. over p.o.administration but there are suggestions of a faster onset of actic In one study i.v. citalopram showed superior response rates over p.o. citalopr (79% vs. 63%) in severely depressed patients at 8 weeks. Copyright 2004 Wi Liss, Inc.

PMID: 14978779 [PubMed - in process]

1: Prog Brain Res. 2002;139:197-210.

Nonpeptide vasopressin receptor antagonists: development of selective and orally active V1a, V2 and V1b receptor ligands.

Serradeil-Le Gal C, Wagnon J, Valette G, Garcia G, Pascal M, Maffrand JP, Le Fur G.

Exploratory Research Department, Sanofi-Synthelabo Recherche, 195 Route d'Espagne 31036 Toulouse, France. claudine.serradeil@sanofi-synthelabo.co

The involvement of vasopressin (AVP) in several pathological states has bee reported recently and the selective blockade of the different AVP receptors c offer new clinical perspectives. During the past few years, various selective, orally active AVP V1a (OPC-21268, SR49059 (Relcovaptan)), V2 (OPC-31 OPC-41061 (Tolvaptan), VPA-985 (Lixivaptan), SR121463, VP-343, FR-161282) and mixed V1a/V2 (YM-087 (Conivaptan), JTV-605, CL-385004) receptor antagonists have been intensively studied in various animal models have reached, Phase IIb clinical trials for some of them. For many years now laboratory has focused on the identification of nonpeptide vasopressin antagonists with suitable oral bioavailability. Using random screening on sm molecule libraries, followed by rational SAR and modelization, we identifiec chemical series of 1-phenylsulfonylindolines which first yielded SR49059, a receptor antagonist prototype. This compound displayed high affinity for ani and human V1a receptors and antagonized various V1a AVP-induced effects vitro and in vivo (intracellular [Ca2+] increase, platelet aggregation, vascula smooth muscle cell proliferation, hypertension and coronary vasospasm). We and others have used this compound to study the role of AVP in various anin models. Recent findings from clinical trials show a potential interest for SR49059 in the treatment of dysmenorrhea and in Raynaud's disease. Structu modifications and simplifications performed in the SR49059 chemical series yielded highly specific V2 receptor antagonists (N-arylsulfonyl-oxindoles), amongst them SR121463 which possesses powerful oral aquaretic properties various animal species and in man. SR121463 is well-tolerated and dose-dependently increases urine output and decreases urine osmolality. It induces free water-excretion without affecting electrolyte balance in contrast to classi diuretics (e.g. furosemide and hydrochlorothiazide). Notably, in cirrhotic rats with ascites and impaired renal function, a 10-day oral treatment with SR121 (0.5 mg/kg) totally corrected hyponatremia and restored normal urine excreti This compound also displayed interesting new properties in a rabbit model o

ocular hypertension, decreasing intraocular pressure after single or repeated instillation. Thus, V2 receptor blockade could be of interest in several water-retaining diseases such as the syndrome of inappropriate antidiuretic hormon secretion (SIADH), liver cirrhosis and congestive heart failure and deserves t widely explored. Finally, further chemical developments in the oxindole fam have led to the first specific and orally active V1b receptor antagonists (with SSR149415 as a representative), an awaited class of drugs with expected therapeutic interest mainly in ACTH-secreting tumors and various emotional diseases such as stress-related disorders, anxiety and depression. However, fi the recently described tissue localization for this receptor, we could also speculate on other unexpected uses. In conclusion, the development of AVP receptor antagonists is a field of intensive pharmacological and clinical investigation. Selective and orally active compounds are now available to giv new insight into the pathophysiological role of AVP and to provide promisin drugs.

Publication Types:

- Review
- Review, Tutorial

PMID: 12436936 [PubMed - indexed for MEDLINE]

Form PTO-1449 U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 1795/62163-AA/ JPW / ANX	Serial No. Not Yet Known 10/723,961
INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)	Applicants Thomas Blackburn, et al.	
	Filing Date Herewith 11/26/03	Group Art Unit ~~Not Yet Known~~ 1624

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Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
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	US	5,801,150	9/1/98	Caillot, et al.	—	—	—
	US	5,728,704	3/17/98	Mylari, et al.	—	—	—
	US	5,547,949	8/20/96	Maho, et al.	—	—	—
	US	5,017,466	5/21/91	Kobayashi, et al.	—	—	—
	US	4,921,503	5/1/90	Anderson, et al.	—	—	—
	US	4,874,687	10/17/89	Itabashi, et al.	—	—	—
	US	4,946,956	8/7/90	Wheeler, et al.	—	—	—
	US	6,368,812	4/9/02	Bard, et al. *	—	—	—

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	WO 99/65875	12/23/99	PCT	—	—	—	—
	WO 99/50251	10/7/99	PCT	—	—	—	—
	WO 99/41253	8/19/99	PCT	—	—	—	—
	WO 93/25539	12/23/93	PCT	—	—	—	—
	EP 0972770	1/19/00	EPO	—	—	—	—
	EP 0945445	9/29/99	EPO	—	—	—	—
	EP 0787809	8/13/97	EPO	—	—	—	—
	EP 0667396	8/16/95	EPO	—	—	—	—
	EP 0659759	3/1/95	EPO	—	—	—	—
	EP 0366633	4/11/90	EPO	—	—	—	—
	EP 0359594	3/21/90	EPO *	—	—	—	—
	JP 07-548	3/14/02	Japan	—	—	—	—
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	JP 11-158703	6/22/77	Japan	—	—	—	—

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	Filing Date Herewith	Group Art Unit Not Yet Known

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		Hokfelt, T., et al., "Galanin and NPY, Two Peptides with Multiple Putative Roles in the Nervous System," Horm. Metab. Res. (1999); 31: 330-334;
		Razani, H., et al., "Intraventricular Galanin Produces a Time-Dependent Modulation of 5-HT1A Receptors in the Dorsal Raphe of the Rat", Neuropharmacology and Neurotoxicology. (2000); 11(18): 3943-3948;
		Chemical Abstracts Registry No. 61038-64-0;
		Chemical Abstracts Registry No. 41230-77-7;
		Chemical Abstracts Registry No. 130186-15-1;
		Chemical Abstracts Registry No. 130186-16-2;
		Chemical Abstracts Registry No. 130186-17-3;
		Chemical Abstracts Registry No. 130186-18-4;
		Chemical Abstracts Registry No. 130186-21-9;
		Chemical Abstracts Registry No. 130270-13-2;
		Chemical Abstracts Registry No. 133939-75-0;
		Chemical Abstracts Registry No. 56984-58-8;
		Chemical Abstracts Registry No. 77910-42-0;
		Chemical Abstracts Registry No. 70010-41-2;
		Chemical Abstracts Registry No. 189264-35-5;
		Chemical Abstracts Registry No. 88291-04-7;
		Chemical Abstracts Registry No. 88291-07-0;
		Chemical Abstracts Registry No. 154118-05-5;
		Chemical Abstracts Registry No. 155717-81-0;
		Chemical Abstracts Registry No. 155717-82-1;
		Chemical Abstracts Registry No. 159967-24-5;

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		Chemical Abstracts Registry No. 136647-72-8;
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		Chemical Abstracts Registry No. 43002-26-2;
		Chemical Abstracts Registry No. 303954-69-2;
		Chemical Abstracts Registry No. 122725-53-5;
		Chemical Abstracts Registry No. 122803-89-8;
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		Chemical Abstracts Registry No. 303149-08-8;
		Chemical Abstracts Registry No. 303149-06-6;
		Chemical Abstracts Registry No. 303984-47-6;
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		Chemical Abstracts Registry No. 303149-12-4;
		Chemical Abstracts Registry No. 303984-51-2;
		Chemical Abstracts Registry No. 303984-49-8;
		Chemical Abstracts Registry No. 303954-48-7;
		Chemical Abstracts Registry No. 303984-52-3;
		Chemical Abstracts Registry No. 303984-60-3;
		Chemical Abstracts Registry No. 303984-61-4;
		Chemical Abstracts Registry No. 303984-62-5;
		Chemical Abstracts Registry No. 303984-68-1;
		English Language Abstract for Japanese Patent No. JP 11,158,073;
		U.S. Serial No. 10/214,873 (Konkel et al.), filed August 7, 2002; NOW ABN
		U.S. Serial No. 10/066,175, filed January 31, 2002, NOW ABN (Exhibit 1).

EXAMINER	DATE CONSIDERED
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